EXPERIENCE WITH PAIRED PACING IN EXPERIMENTAL CANINE HEART FAILURE*

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OUR interest in paired pacing and postextrasystolic potentiation was aroused by a report from Dr. William Chardack on work in which the technique was used to control the ventricular rate. A visit by Dr. Brian Hoffman to our laboratory was the direct stimulus for the following work.

This report is concerned with the effects of paired pacing on experimental heart failure in dogs. A total of 20 animals was used. All were open-chest experiments in which ventilation was maintained by intermittent positive pressure.** Rigid catheters were placed in the right atrium, the left ventricle, and the ascending aorta. Pressures were measured by Statham strain gauges and monitored on a multichannel oscilloscope.† Aortic flow was measured by a calibrated electromagnetic flowmeter‡ and integrated with time. The dp/dt of the left ventricular pressure was recorded. In 18 of the 20 dogs, heart block was produced by cutting the conduction bundle medial to the coronary sinus ostium. Heart block was produced to ease the control of the heart rate under varying experimental conditions. The electrical stimuli were delivered by Teflon-coated wires sutured into the avascular portions of the left ventricle near its apex. The stimuli were delivered by a Medtronic coupled pulse generator (Model No. 5830), a Tektronix impulse generator and, later, by the Medtronic "R" wave coupled-pulse generator (Model No. 5837††). The ventricular rate was kept constant in 18 experiments at 112/min. during single and paired pacing.

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**Ventilator made by G. F. Palmer, Ltd., Effra Road, London, S. W. 2.
†Electronics for Medicine, White Plains, N. Y.
‡Carolina Medical Electronics, Inc., Winston-Salem, N. C.
††Medtronic, Inc., Minneapolis, Minn.

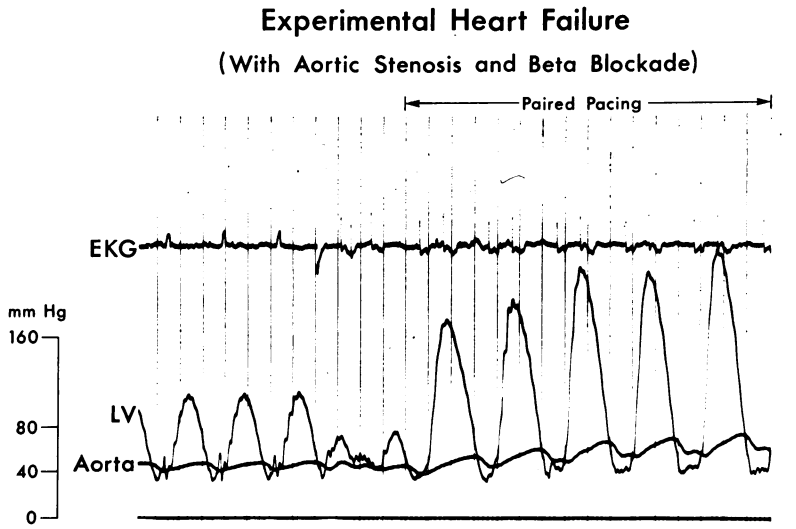

Fig. 1. Effects of paired pacings on aortic and left ventricular pressures in a dog with heart failure produced by aortic constriction and beta-adrenergic blockade with Inderal.

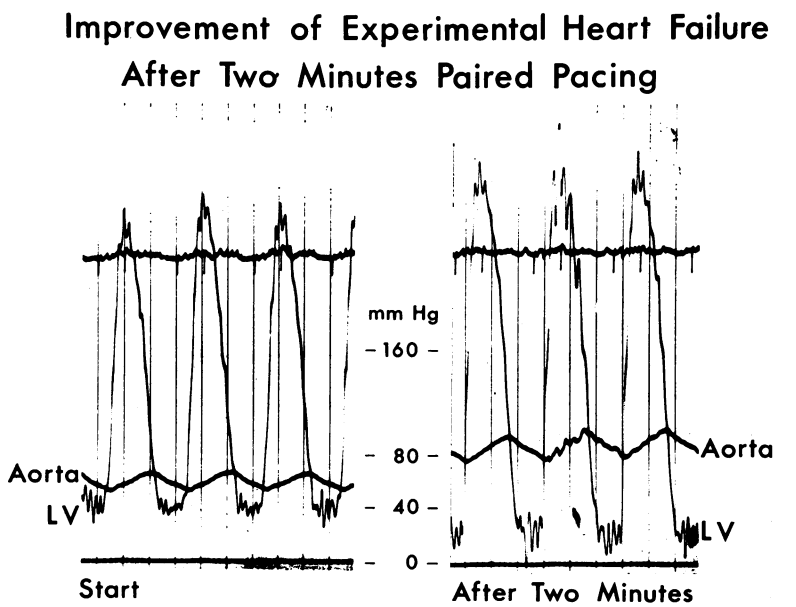

Fig. 2. Improvement in canine heart failure with paired pacing. Note the increase in aortic and left ventricular systolic pressures with prolongation of the paired pacing. The left ventricular end-diastolic pressure dropped from 40 mm. Hg to 15 mm. Hg after two minutes of paired pacing, reflecting the improvement in cardiac performance.

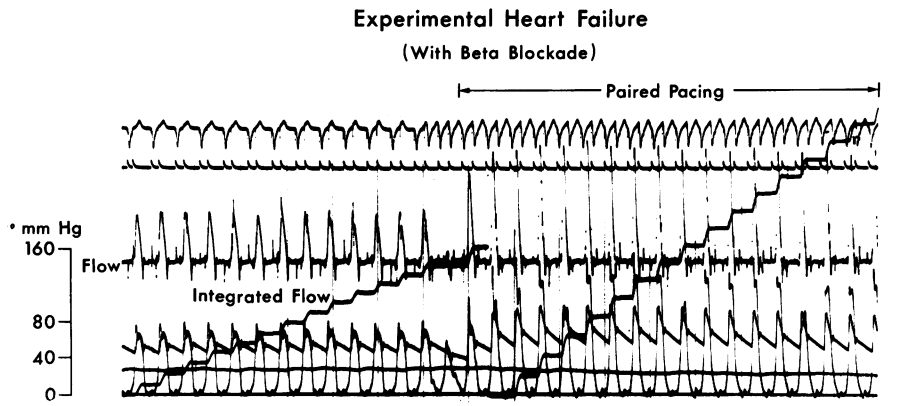

Fig. 3. Effects of changing from single pacing to paired pacing in a continuous record. The heart failure was achieved by administration of large doses (2 mg./kg.) of the beta-blocking agent Inderal. In this instance a 90 per cent increase in aortic flow occurred with paired pacing. Ventricular rate was constant at 112/min. during single and paired pacing.

Heart failure was produced by aortic constriction and the administration of a beta-adrenergic blocking agent (Inderal†). This agent not only blocks the action of the catecholamines but, in higher dosage, has a marked negative inotropic effect on heart muscle.

Our experience is confirmation of much that has been presented in this conference. Paired pacing results in marked postextrasystolic potentiation of myocardial contractility. Figure 1 illustrates this in a preparation with severe left ventricular failure induced by aortic constriction and Inderal. In heart failure of this type, paired pacing led not only to an increase in left ventricular systolic pressure and aortic pressure but to a decrease in left ventricular end-diastolic pressure. With persistence of paired pacing the improvement in cardiac behavior usually continues, as illustrated in Figure 2.

Paired pacing consistently increased the cardiac output when heart failure was present. Figure 3 shows a 90 per cent increase in aortic flow occurring with paired pacing over single pacing at the same ventricular rate. The heart failure in this experiment was produced by the administration of 2 mg./kg. of Inderal.® When the cardiac output is normal, paired pacing causes only slight or no increase in output (Figure 4). In this respect the postextrasystolic potentiation (PESP) resembles the behavior of digitalis in which the inotropic action may not be manifest

†Obtained from Ayerst Laboratories, New York, N. Y.

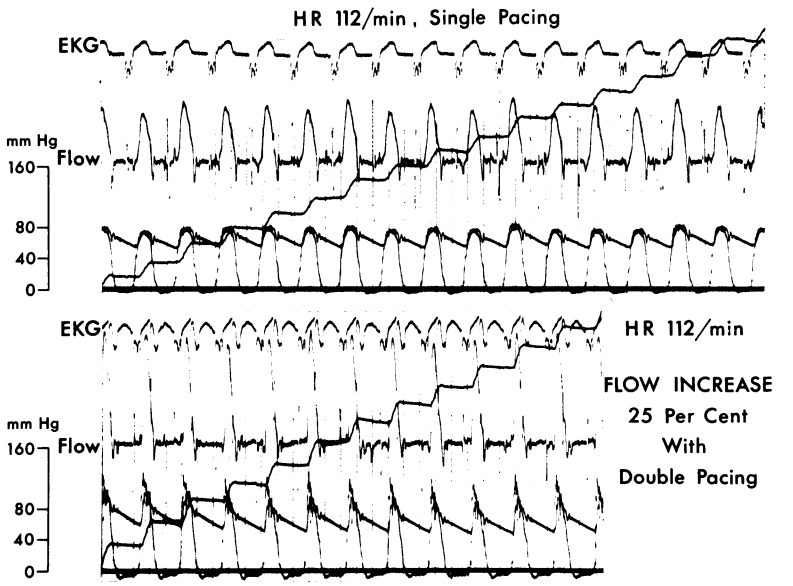

Fig. 4. Effects of single and paired pacing on aortic flow in a dog with complete heart block. No heart failure was present. In this experiment aortic flow increased by only 25 per cent with paired pacing.

unless heart failure is present. It is worth noting that we also found the PESP of paired pacing occurring in animals that had received large doses of ouabain. This suggests that the augmentation of myocardial contractility of PESP has a mechanism different from that of digitalis.

PESP resembles the action of epinephrine and isoproterenol on myocardial contractility in increasing the vigor of contraction as reflected in the dp/dt of the ventricular pressure pulse (Figure 5). However, PESP will occur in the absence of catecholamines and in chemical blockade of these substances. It is apparent, therefore, that PESP acts independently of catecholamine action.

The increase in cardiac output with paired pacing is not a transient phenomenon but can be maintained for long periods, as others have reported in this conference. PESP can be produced in very severely depressed hearts. In several experiments the heart failure was so severe that with single pacing the dog heart would go into ventricular fibrillation. Following electrical defibrillation and massage, paired pacing was able to produce adequate cardiac outputs.

In eight experiments, coronary flow and myocardial oxygen con-

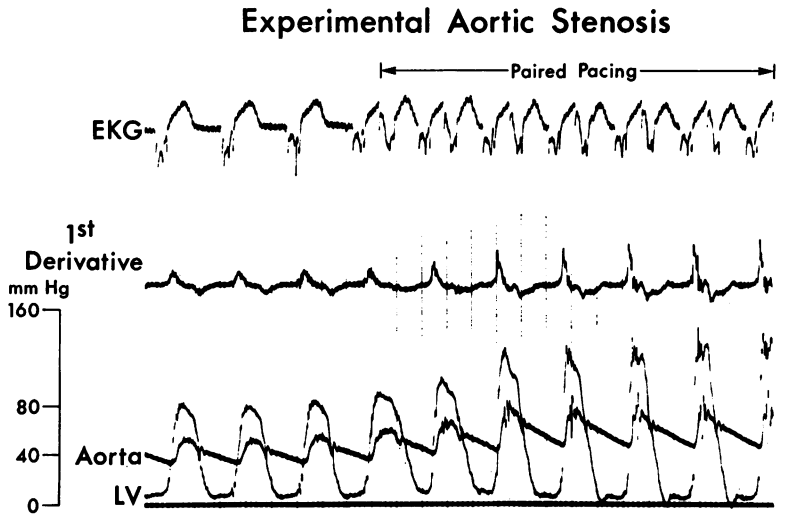

Fig. 5. Effect of going from single pacing to paired pacing at a constant ventricular rate in dog with complete heart block and aortic stenosis. Note the immediate increase in ventricular contractility in the first beat of paired pacing. The augmentation of ventricular contractility is evidenced by the increase in the left ventricular and aortic pressure and in the first derivative of the left ventricular pressure pulse. PESP resembles the behavior of epinephrine but will occur with beta-adrenergic blockade.

sumption were measured. This was accomplished by cannulation of the coronary sinus and direct measurement of coronary sinus flow in a graduate cylinder for short periods. The oxygen content of the coronary sinus blood and the aortic blood was determined by the Van Slyke technique. Paired pacing when compared to single pacing always resulted in an increase in coronary sinus flow and myocardial oxygen consumption. This is to be expected, as more work is done with paired pacing. The oxygen cost of paired pacing is not excessive. In one experiment in which heart failure was not present, cardiac output, stroke volume, coronary flow, and myocardial oxygen consumption were measured when the animal was in sinus rhythm at a rate of 165 and, during paired pacing, at a rate of 112/min. In this experiment the cardiac output was identical, the coronary flow was slightly less with paired pacing, and myocardial oxygen consumption was definitely less with paired pacing as compared with sinus rhythm at a faster heart rate. The coronary flow and myocardial oxygen consumption were consistently greater with paired pacing than with single pacing in our ani-

mals in heart failure. The cardiac outputs were also greater with paired pacing. If one relates myocardial oxygen consumption to cardiac output, then there is no difference in these two groups in this respect. These observations, plus the experience that PESP can be maintained for prolonged periods, is strong evidence that the metabolic cost of PESP is not excessive.

We have experience with six human cases. The first two were moribund patients following cardiac arrest whom we were unable to resuscitate. Paired pacing strengthened ventricular contraction in both but not enough for prolonged survival. We successfully used the technique in two patients in the operating room just prior to going on cardiopulmonary bypass. Two patients were studied in the cardiac catheterization laboratory. The first was an elderly man with complete heart block in severe congestive heart failure. With a venous catheter we had difficulty in capturing the beat effectively. We finally did, but could achieve only a one-to-one response between QRS and ventricular contraction. This led to ventricular tachycardia, which persisted when the stimulation was discontinued. The ventricular tachycardia was controlled by countershock. The second patient studied in the cardiac catheterization laboratory also had complete heart block with implanted myocardial electrodes and pacemaker failure. This study was done immediately before his pacemaker generator was changed. Stimulation was applied through the myocardial electrodes through a small abdominal incision. Paired pacing was easily accomplished in this patient. Cardiac output, which was normal, did not change during single and paired pacing. It is of interest that a significant change occurred in his right ventricular end-diastolic pressure with paired pacing dropping from 10 mm. Hg to 5 mm. Hg. The cardiac output was measured 16 minutes after initiation of paired pacing. It is possible that we missed an early increase in the cardiac output at the beginning of the paired pacing. It is also possible, as Dr. Herbert Bartelstone suggests, that PESP may result in increased ventricular compliance. On several occasions this patient experienced angina when we were attempting to capture him with paired pacing. This occurred when the second of the stimuli produced discrete but ineffective ventricular contractions, so that no aortic flow resulted. The angina disappeared when the second stimulus was moved closer to the first stimulus of the pair, resulting in no effective ventricular contraction with the second of the pair.